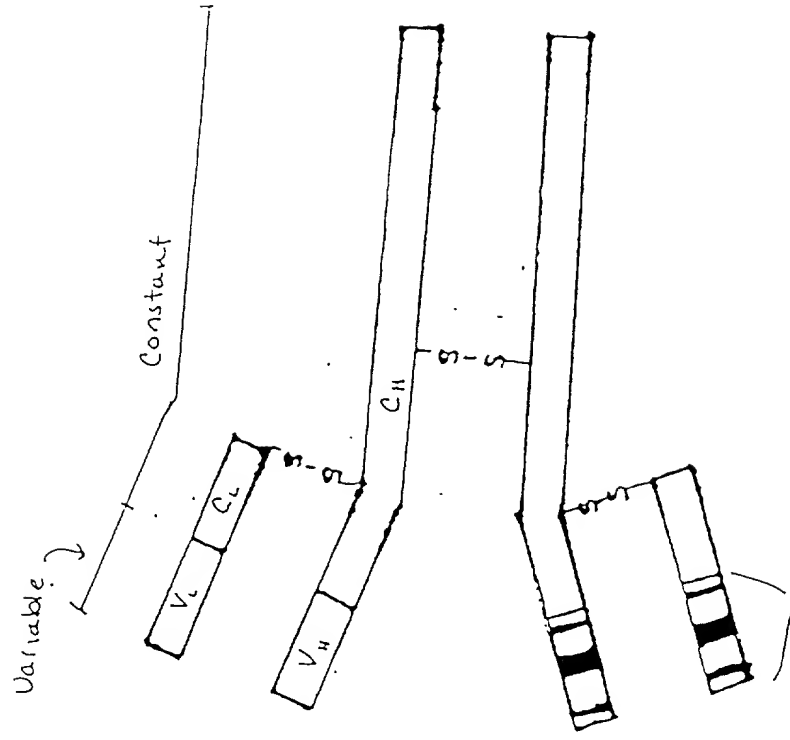




FIGURE 2



Hypervariable regions  
Containing 3 CDRs

FIGURE 3

Effect of Anti-Staph MAB 96-110 on Survival in a Lethal *S. aureus* Sepsis Model

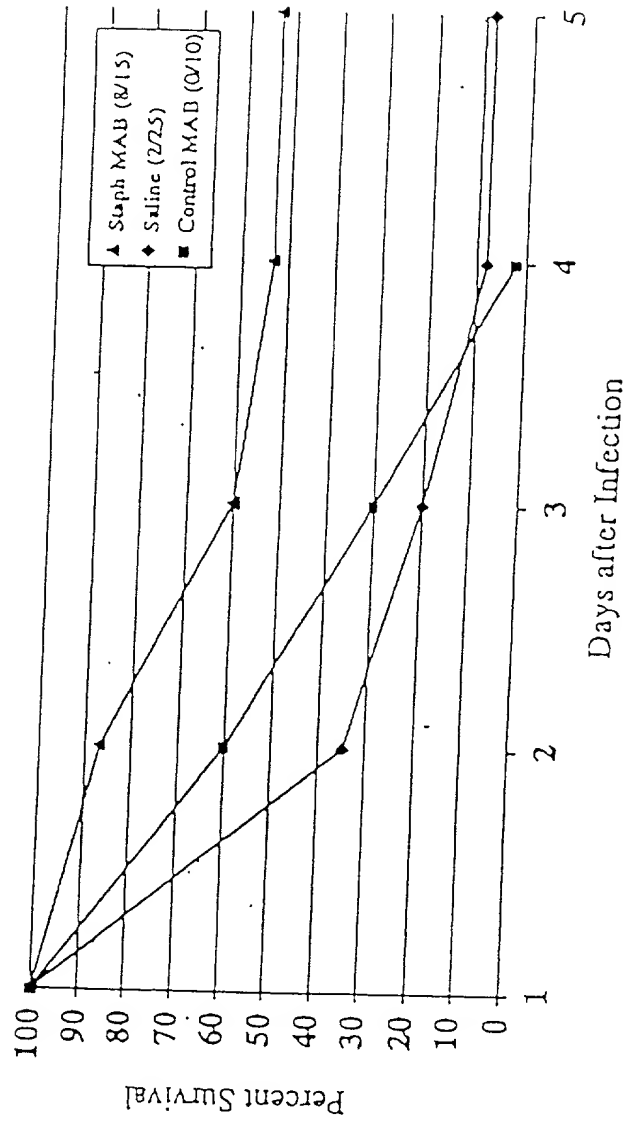


FIGURE 4

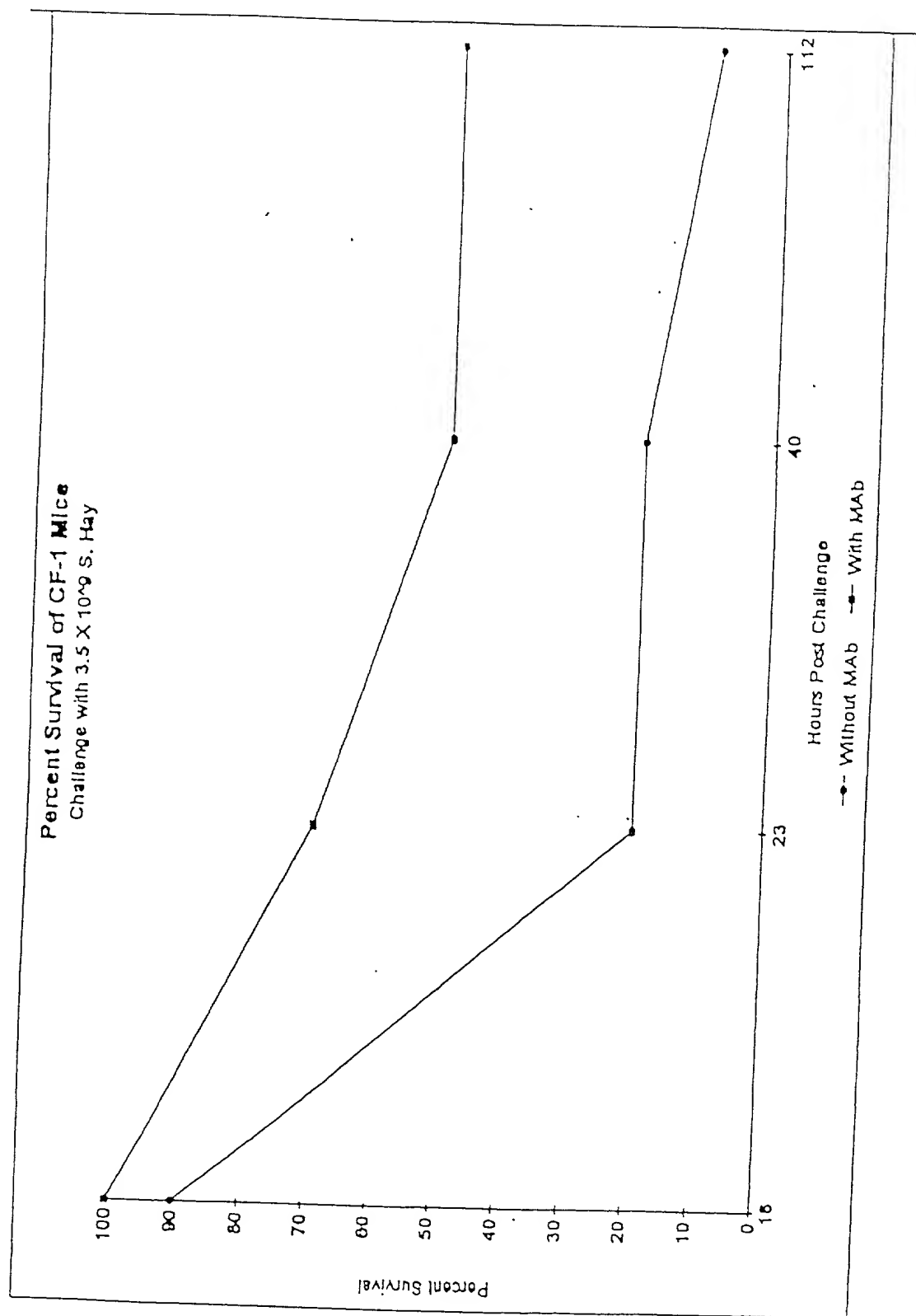


FIGURE 5

6MER.SEQ		10	20	30	
11	13.6mer2-1	GGGGCTCATC	CGGATAGGGT	TTATGGGGCC	SEQ ID NO. 4
61		C A H A D R V	Y G A		SEQ ID NO. 5
12	14.6mer2-2	GGGGCTCATC	CGGATAGGGT	TTATGGGGCC	
65		G A H A D R V	Y G A		
13	15.6mer2-3	GGGGCTCATC	CGGATAGGGT	TTATGGGGCC	
66		G A H A D R V	Y G A		
14	16.6mer2-4	GGGGCTCATC	CGGATAGGGT	TTATGGGGCC	SEQ ID NO. 6
62		G A H A D R V	Y G A		SEQ ID NO. 7
15	17.6mer2-5	GGGGCTCATC	CGGATAGGGT	TTATGGGGCC	
67		G A H A D R V	Y G A		
16	18.6mer2-6	GGGGCTCATC	CGGATAGGGT	TTATGGGGCC	
68		G A H A D R V	Y G A		
17	19.6mer2-7	GGGGCTCATC	CGGATAGGGT	TTATGGGGCC	
69		G A H A D R V	Y G A		
18	20.6mer2-8	GGGGCTCATC	CGGATAGGGT	TTATGGGGCC	
70		G A H A D R V	Y G A		
19	21.6mer2-9	GGGGCTCATC	CGGATAGGGT	TTATGGGGCC	
71		G A H A D R V	Y G A		
51	23.6mer2-1	GGGGCTCATC	CGGATAGGGT	TTATGGGGCC	
72		G A H A D R V	Y G A		
52	24.6mer2-1	GGGGCTCATC	CGGATAGGGT	TTATGGGGCC	
73		G A H A D R V	Y G A		
53	25.6mer2-1	GGGGCTCATC	CGGATAGGGT	TTATGGGGCC	
74		G A H A D R V	Y G A		
54	26.6mer2-1	GGGGCTCATC	CGGATAGGGT	TTATGGGGCC	
75		G A H A D R V	Y G A		
55	27.6mer2-1	GGGGCTCATC	CGGATAGGGT	TTATGGGGCC	
76		G A H A D R V	Y G A		
56	28.6mer2-1	GGGGCTCATC	CGGATAGGGT	TTATGGGGCC	
77		G A H A D R V	Y G A		
58	30.6mer2-1	GGGGCTCATC	CGGATAGGGT	TTATGGGGCC	
78		G A H A D R V	Y G A		
59	31.6mer2-1	GGGGCTCATC	CGGATAGGGT	TTATGGGGCC	
79		G A H A D R V	Y G A		
60	32.6mer2-2	GGGGCTCATC	CGGATAGGGT	TTATGGGGCC	
80		G A H A D R V	Y G A		

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[illegible]

15MER1 SEQ		10	20	30	40	50	60	
17	28.15mer1-2/	GGGGCTGATT	CGATTACTTT	TCATCGTCGT	CATCATGATC	GTGTTCTTTC	TGGGGCC	SEQ ID NO. 44
		C A D	(W) I T F	(H) R R	H (H) D	(R) V L S	G A	SEQ ID NO. 45
18	29.15mer1-3/	GGGGCTGGTT	GGATTACTTT	TCATCGTCGT	CATCATGATC	GTGTTCTTTC	TGGGGCC	SEQ ID NO. 46
		G A C	W I T F	H R R	H H D	R V L S	G A	SEQ ID NO. 47
19	32.15mer1-6/	GGGGCTGGTT	GGATTACTTT	TCATCGTCGT	CATCATGATC	GTGTTCTTTC	TGGGGCC	
		G A G	W I T F	H R R	H H D	R V L S	G A	
20	33.15mer1-7/	GGGGCTGGTT	GGATTACTTT	TCATCGTCGT	CATCATGATC	GTGTTCTTTC	TGGGGCC	
		G A G	W I T F	H R R	H H D	R V L S	G A	
21	34.15mer1-8/	GGGGCTGGTT	GGATTACTTT	TCATCGTCGT	CATCATGATC	GTGTTCTTTC	TGGGGCC	
		G A G	W I T F	H R R	H H D	R V L S	G A	
22	35.15mer1-9/	GGGGCTGGTT	GGATTACTTT	TCATCGTCGT	CATCATGATC	GTGTTCTTTC	TGGGGCC	
		C A G	W I T F	H R R	H H D	R V L S	G A	
23	36.15mer1-10/	GGGGCTGGTT	GGATTACTTT	TCATCGTCGT	CATCATGATC	GTGTTCTTTC	TGGGGCC	
		G A G	W I T F	H R R	H H D	R V L S	G A	
24	37.15mer1-11/	GGGGCTGGTT	GGATTACTTT	TCATCGTCGT	CATCATGATC	GTGTTCTTTC	TGGGGCC	
		C A C	W I T F	H R R	H H D	R V L S	G A	
25	38.15mer1-12/	GGGGCTGGTT	GGATTACTTT	TCATCGTCGT	CATCATGATC	GTGTTCTTTC	TGGGGCC	
		C A C	W I T F	H R R	H H D	R V L S	G A	
26	39.15mer1-13/	GGGGCTGGTT	GGATTACTTT	TCATCGTCGT	CATCATGATC	GTGTTCTTTC	TGGGGCC	
		C A C	W I T F	H R R	H H D	R V L S	G A	
27	40.15mer1-14/	GGGGCTGGTT	GGATTACTTT	TCATCGTCGT	CATCATGATC	GTGTTCTTTC	TGGGGCC	
		G A G	W I T F	H R R	H H D	R V L S	G A	
28	41.15mer1-15/	GGGGCTGGTT	GGATTACTTT	TCATCGTCGT	CATCATGATC	GTGTTCTTTC	TGGGGCC	
		G A G	W I T F	H R R	H H D	R V L S	G A	
29	42.15mer1-16/	GGGGCTGGGA	AGGCTATGTT	TACTCATCTT	TATCGTCATC	GGGCTTCGGC	TGGGGCC	SEQ ID NO. 48
		G A G	(K) A M F	(S) H S	Y R (H)	(R) G S A	G A	SEQ ID NO. 49
30	23.15mer1-17/	GGGGCTGGTT	GGATTACTTT	TCATCGTCGT	CATCATGATC	GTGTTCTTTC	TGGGGCC	
		G A C	W I T F	H R R	H H D	R V L S	G A	
31	24.15mer1-18/	GGGGCTGGTT	GGATTACTTT	TCATCGTCGT	CATCATGATC	GTGTTCTTTC	TGGGGCC	
		C A C	W I T F	H R R	H H D	R V L S	G A	
32	25.15mer1-19/	GGGGCTGGTT	GGATTACTTT	TCATCGTCGT	CATCATGATC	GTGTTCTTTC	TGGGGCC	
		G A G	W I T F	H R R	H H D	R V L S	G A	
33	26.15mer1-20/	GGGGCTGGTT	GGATTACTTT	TCATCGTCGT	CATCATGATC	GTGTTCTTTC	TGGGGCC	
		G A G	W I T F	H R R	H H D	R V L S	G A	





FIGURE 9

Comparison of Signals at  $6.25 \times 10^{11}$  vir/mL.

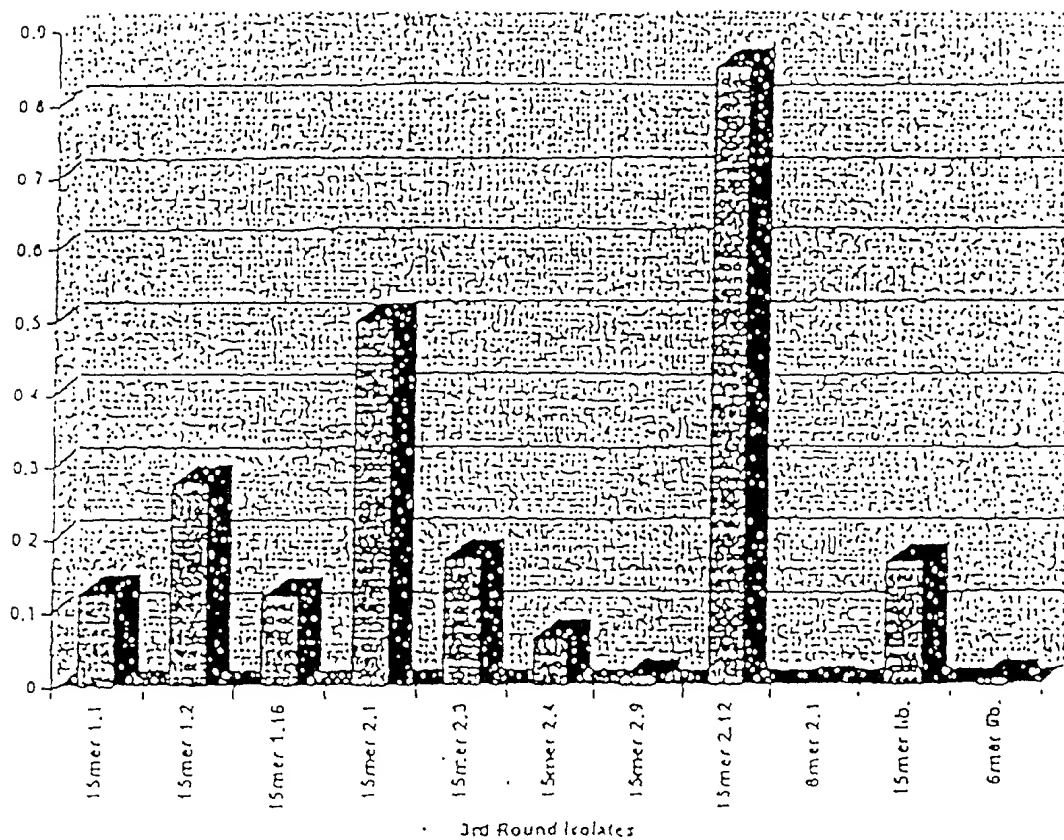
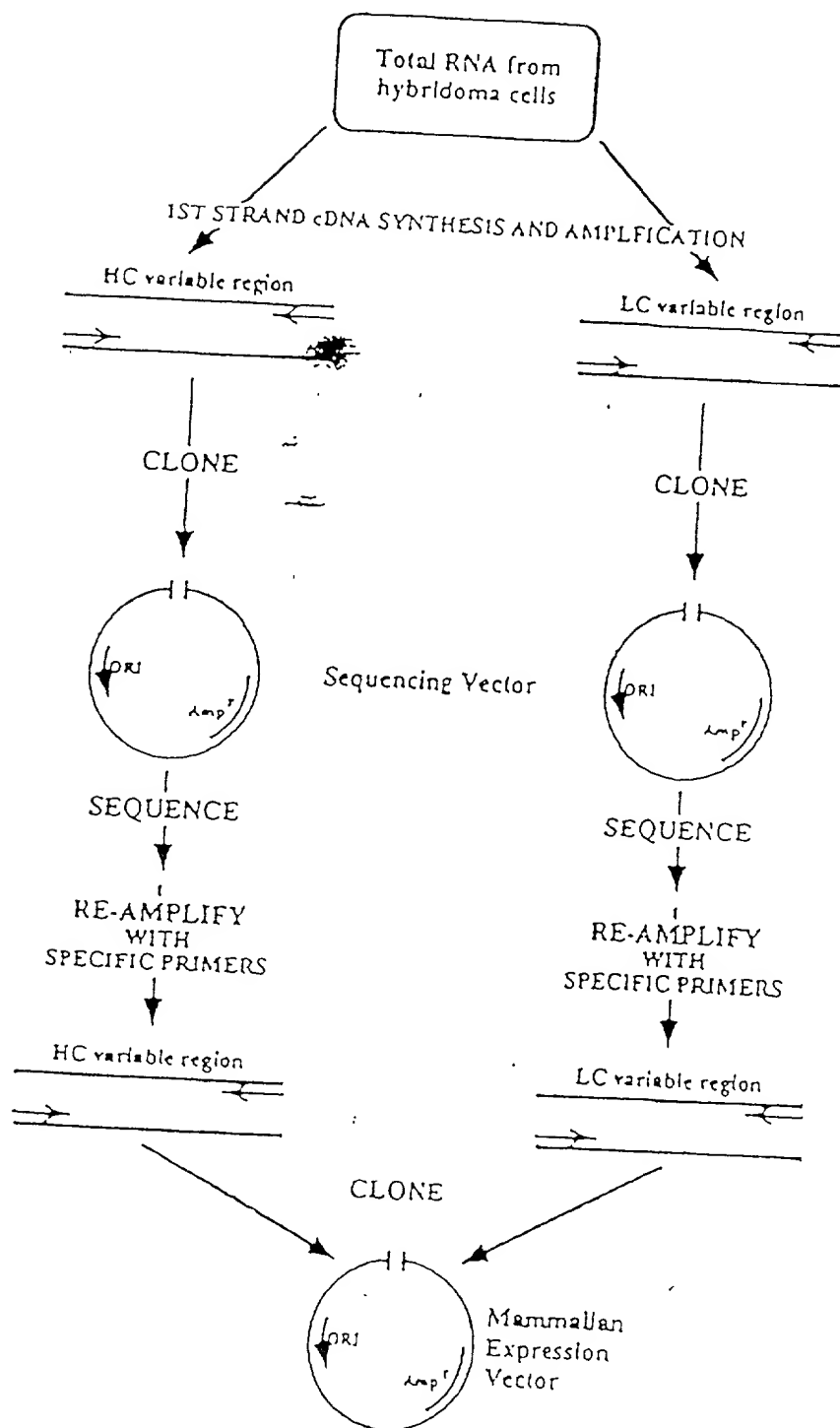


FIGURE 10: General Cloning Strategy



## FIGURE 11

### Mouse Heavy Chain "front" primers

JSS1  
5'-ATTTCAGGCCCCAGCCGGCCATGGCCGARGTRMAGCTKSAKGAGWC-3' SEQ ID NO 68  
JSS2  
5'-ATTTCAGGCCCCAGCCGGCCATGGCCGARGTYCARCTKCARCARYC-3' SEQ ID NO 69  
JSS3  
5'-ATTTCAGGCCCCAGCCGGCCATGGCCGAGGTGAAGCTKSTSGARTC-3' SEQ ID NO 70  
JSS4  
5'-ATTTCAGGCCCCAGCCGGCCATGGCCGAVGTGMWGCTKGTGGAGWC-3' SEQ ID NO 71  
JSS8  
5'-ATTTCAGGCCCCAGCCGGCCATGGCCGAGGTBCARCTKMARSARTC-3' SEQ ID NO 72

### Mouse Heavy chain "back" primers

JS160  
5'-GCTGCCACCGCCACCTGMRGAGACDGTGASTGARG-3' SEQ ID NO 73  
JS161  
5'-GCTGCCACCGCCACCTGMRGAGACDGTGASMTRG-3' SEQ ID NO 74  
JS162  
5'-GCTGCCACCGCCACCTGMRGAGACDGTGASCARG-3' SEQ ID NO 75

### Mouse Light Chain Leader "front" primers

PMC12  
5'-CCCCGGGCCACCATGGAGACAGACACACTCCTG-3' SEQ ID NO 76  
PMC13  
5'-CCCCGGGCCACCATGGATTTTCAAGTGCAGATTTTC-3' SEQ ID NO 77  
PMC14  
5'-CCCCGGGCCACCATGGAGWCACAKWCTCAGGTC-3' SEQ ID NO 78  
PMC15  
5'-CCCCGGGCCACCATGKCCCCWRCTCAGYTTCTKG-3' SEQ ID NO 79  
PMC55  
5'-CCCCGGGCACCATGAAGTTGCCTGTTAGGCTG-3' SEQ ID NO 80

### Mouse Light Chain "back" primer

OXA57  
5'-GCACCTCCAGATGTTAACTGCTC-3' SEQ ID NO 81

### "96-110" Specific Primers

96110HF2  
5'-TAATATTCGGACAGCTACAGGTGTCCACTCCCGAAGTGATGCTGGTGGAGWCTG-3' SEQ ID NO 82  
96110HB  
5'-TTATAGAATTCTGAGGAGACGGTGAGTGAG-3' SEQ ID NO 83  
96110BLF  
5'-TTAGGGCATATCGTCTCTCCAGTCTCC-3' SEQ ID NO 84  
96110BLB  
5'-GTAACCGTTCGAAAAAGTGTACTTACGTTTTATTTCCAGCATGGTCC-3' SEQ ID NO 85

059315-062901  
T96290-5T96290

FIGURE 12

96-110 anti-staph (HAY) heavy chain variable region (type IIIA)

GAAGTCATGCTGGTGGAGTCTGGTGGAGATGGTGGCAGCCTAAAGGTCATTTGAACTCTCATGTGCAAGCTCTGCACTTCAAT 3EQ 1D NO. 86  
 E V M L V E S G G G L V Q P K G S L K L S C A A S G F T F H SEQ 1D NO. 87  
 AACTAGCCCATGAAAT TGGGTCCGCCAGGCTCCAGGAAGGGTTGGAAATGGTTGCT SEQ 1D NO. 88  
 N Y A H N W V R Q A P G K G L E W V A SEQ 1D NO. 89  
 CCAATAGAGAACTAAAGTAATTAATTAAGCAATTTAAAGCCGATTCAGTGAAAGAC SEQ 1D NO. 90  
 R I R S K S N N Y A T P Y A D S V X D SEQ 1D NO. 91  
 AGGTTCAACCATCTCCAGACATGATTCACAAAGCAATGCTCTATCTGCAATGAACTGAACTAGGACACAGCCATGTATTACTGTGTACAG SEQ 1D NO. 92  
 R P T I S R D D S Q S H L Y L Q H N N L K T E D T A H Y Y C V R SEQ 1D NO. 93  
 CCGGGGGCTTCAGGGATTAAGTAACTATGGAATAC TGGGTCAAGGAACCTCACTACCGTCTCTCA SEQ 1D NO. 94  
 R G A S G I D Y A H D Y H G Q G T S L T V S S SEQ 1D NO. 95

96-110 anti-staph (HAY) light chain variable region (type VI)

CAATTTGTTCTCTCCAGTCTCCAGCAATCTCTGTCTGCAATCTCCAGGGGAAAGGTCACAAATGACTTCC SEQ 1D NO. 96  
 Q I V L S Q S P A I L S A S P G E K V T H T C SEQ 1D NO. 97  
 AGGGCCAGCTCAAGCTTAAATTAATACAC SEQ 1D NO. 98  
 R A S S S V N Y H R SEQ 1D NO. 99  
 TGGTACCAGCAGAGCCAGGATCTCTCCCAACCCCTGGATTCT GGCACATCCAACTGGTTCT SEQ 1D NO. 100  
 H Y Q Q Q K P G S S P K P H I S A T S N L A S SEQ 1D NO. 101  
 CGAGTCCCTGCTCGCTTCAGTGGCAATGGGTCTGGAGCCTTACTCTCTCAATCAAGAGTGGAGCTGAAATGCTGCCACTTATTACTCC SEQ 1D NO. 102  
 G V P A R P S G S G S G T S Y S L T I S R V E A E D A A T Y Y C SEQ 1D NO. 103  
 CAGCAGTGGAGTAGTAAGCCAGCCAGC TCCGAGGGGGAGCCATGCTGGAAATAGA SEQ 1D NO. 104  
 Q Q W S S N P P T F G G G T H L E I R SEQ 1D NO. 105

CDR Regions Underlined



FIGURE 14

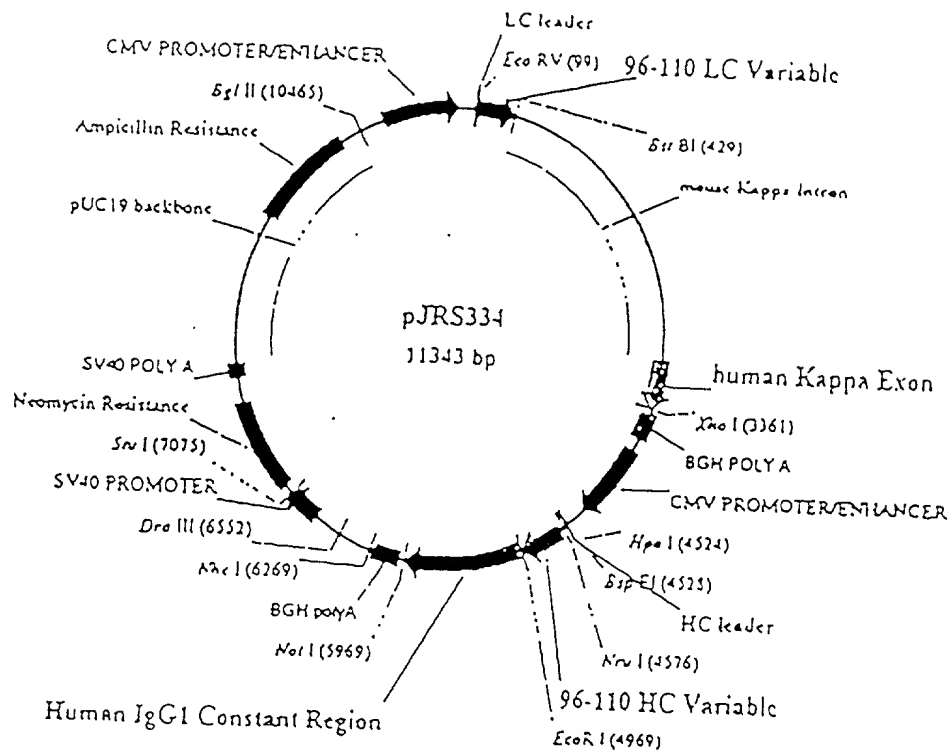


FIGURE 15: Antibody Production ELISA

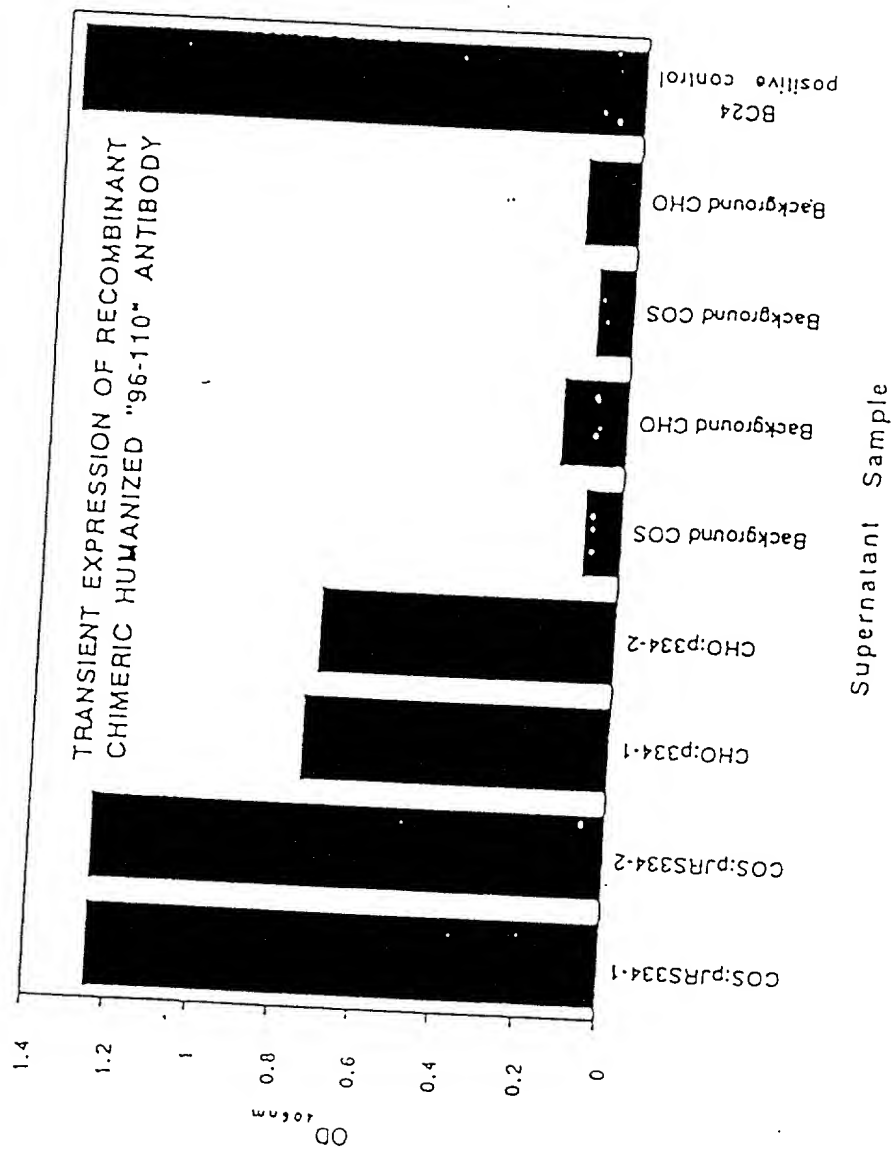
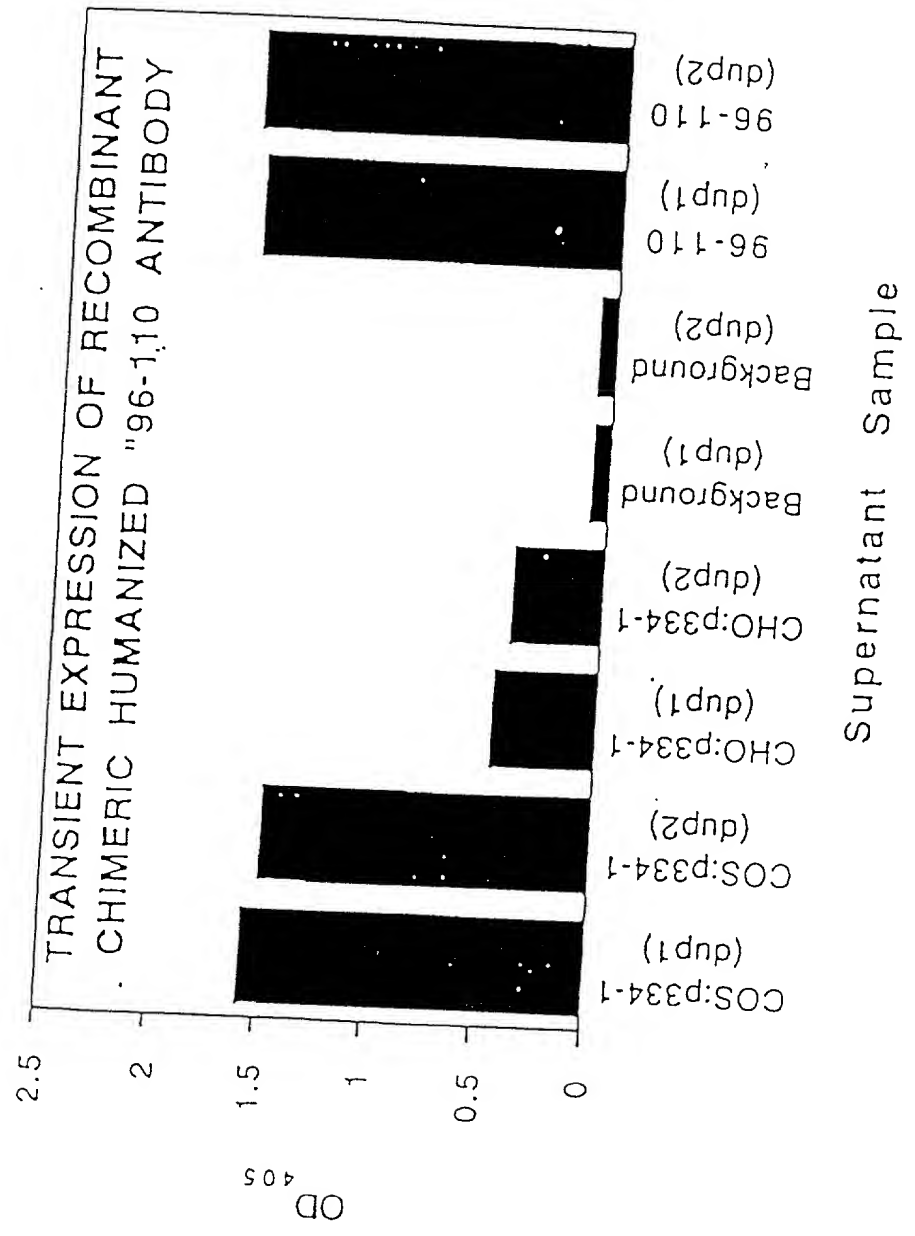
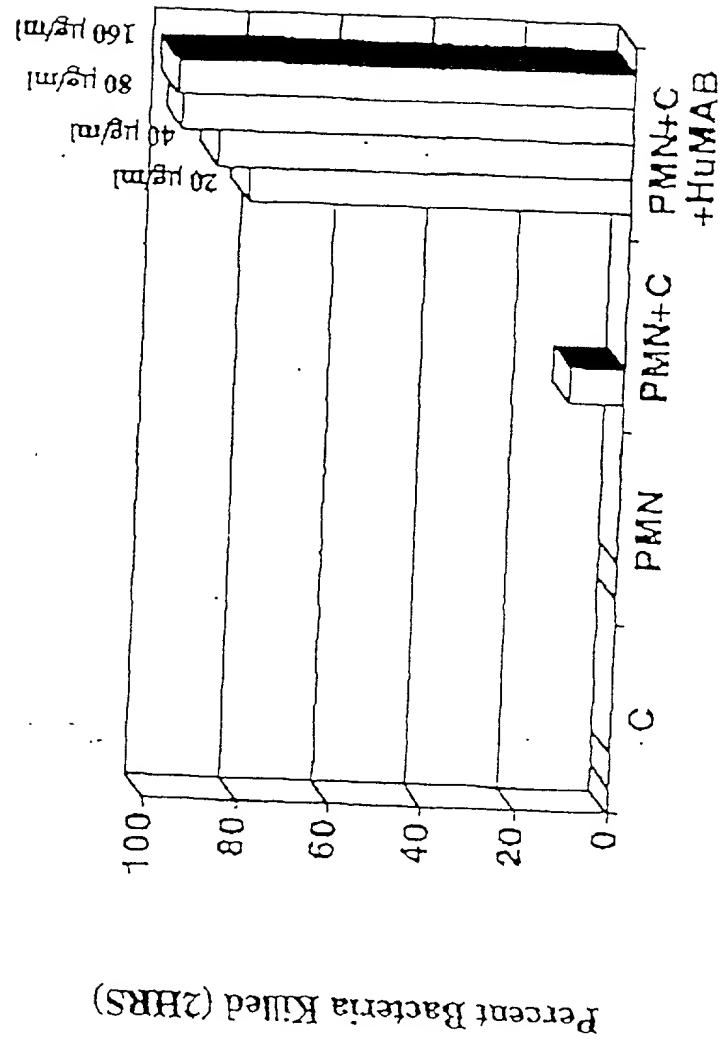


FIGURE 16: Anti-Staph HAY Activity ELISA



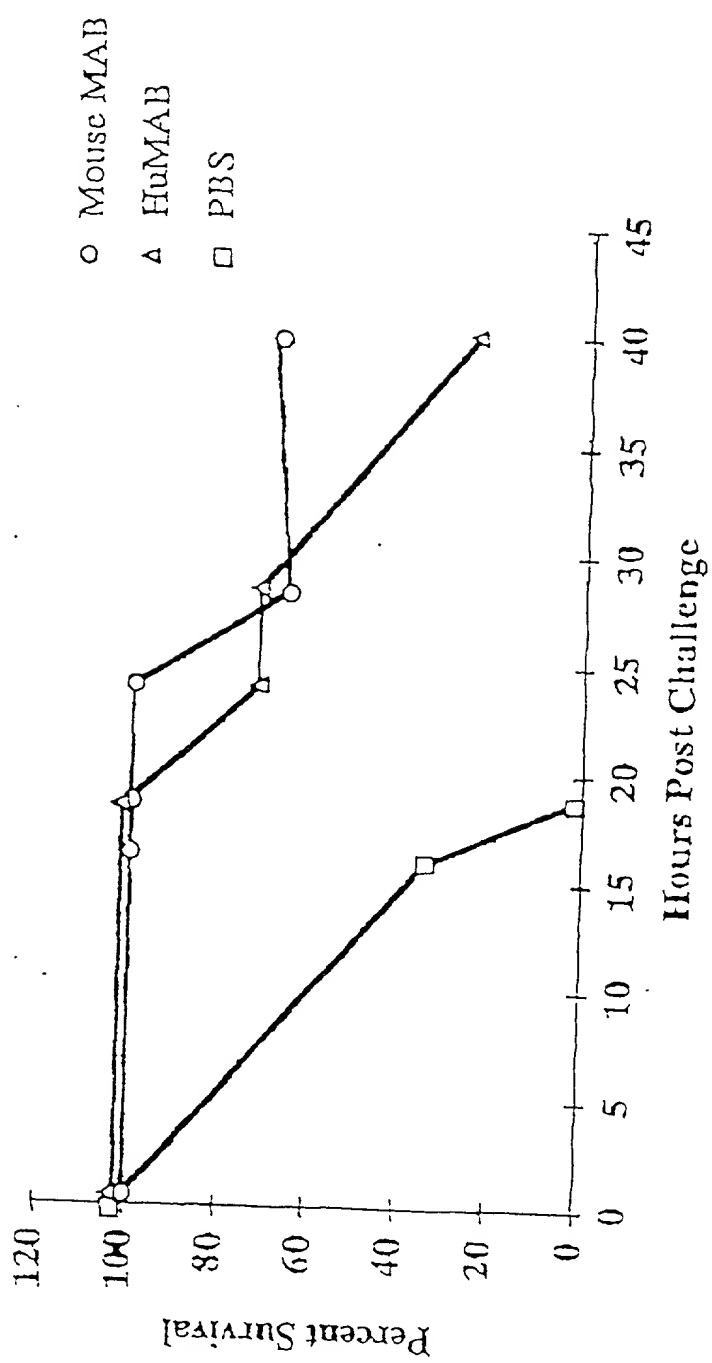


# Opsonic Activity of HuMAB 96-110 for *S.epidermidis* in a Neutrophil Mediated Opsonophagocytic Bactericidal Assay Using Human Complement



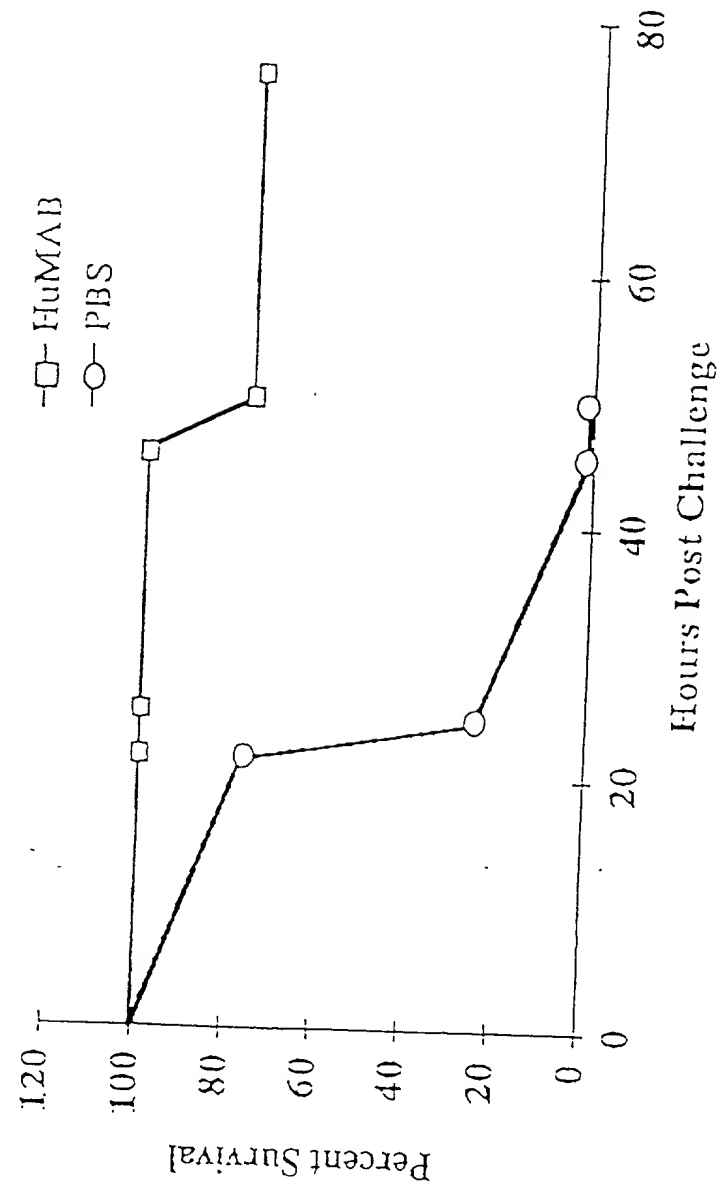
C-Barb-Ex (1:4), Human  
PMN-Human  
Bacteria-*S.epidermidis* (Strain Hay)

Pilot Study to Compare the Effect of Mouse  
MAB 96-110 and HuMAB 96-110 in a Lethal  
Model of *S. Epidermidis* Sepsis



MAB dose: 14 mg/kg given IP, 24 and 1 hour prior to infection

# Survival of CF-1 Mice after Intraperitoneal Challenge with 3x10<sup>9</sup> *S. epidermidis* (Hay)



18 mg/kg/dose, IP, 24 and 1 Hour prior to infection

# Effect of HuMAB 96-110 on Bacteremia in a Lethal *S. epidermidis* Sepsis Model

## Geometric Mean Bacteremia Level

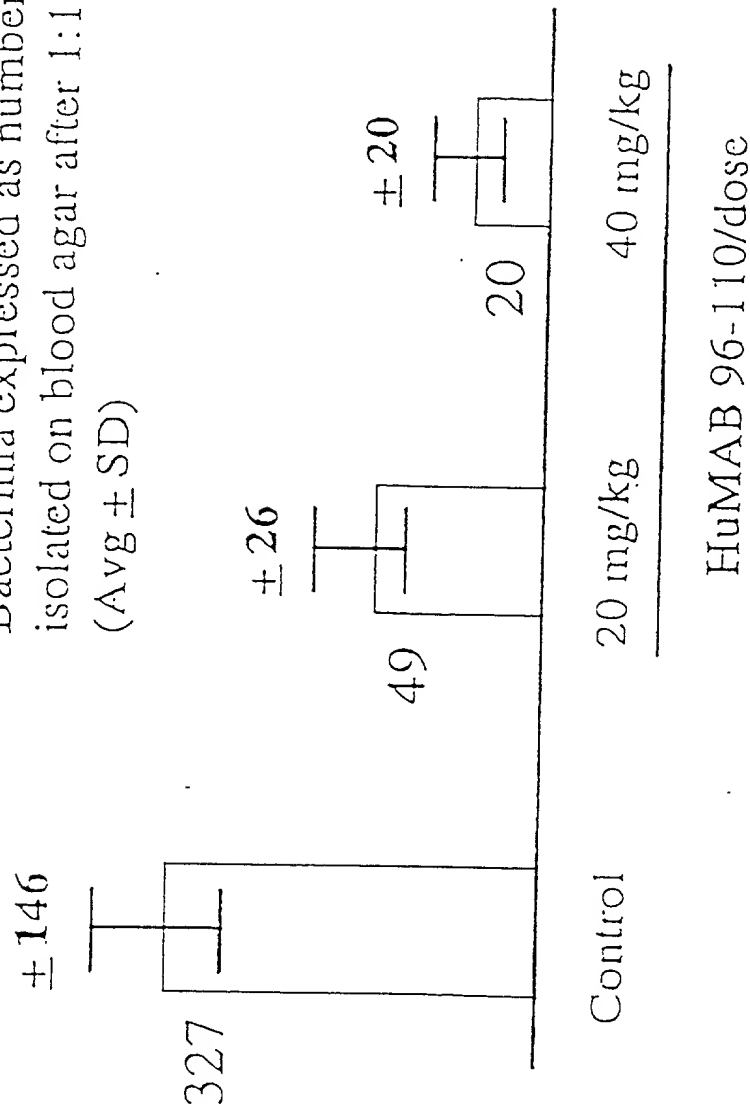
Saline				
Placebo	$6.5 \times 10^4$	$7.2 \times 10^4$	$5.2 \times 10^4$	$7 \times 10^3$
HuMAB				
96-110	$3 \times 10^2$	$7.5 \times 10^2$	$2.1 \times 10^1$	$1.7 \times 10^1$
	4 hrs	8 hrs	12 hrs	18 hrs

## Time Post Infection

HuMAB 96-110 18 mg/kg/dose or saline given IP, 24 and 1 hour prior to IP infection with  $3 \times 10^9$  *S. epidermidis* (Hay)

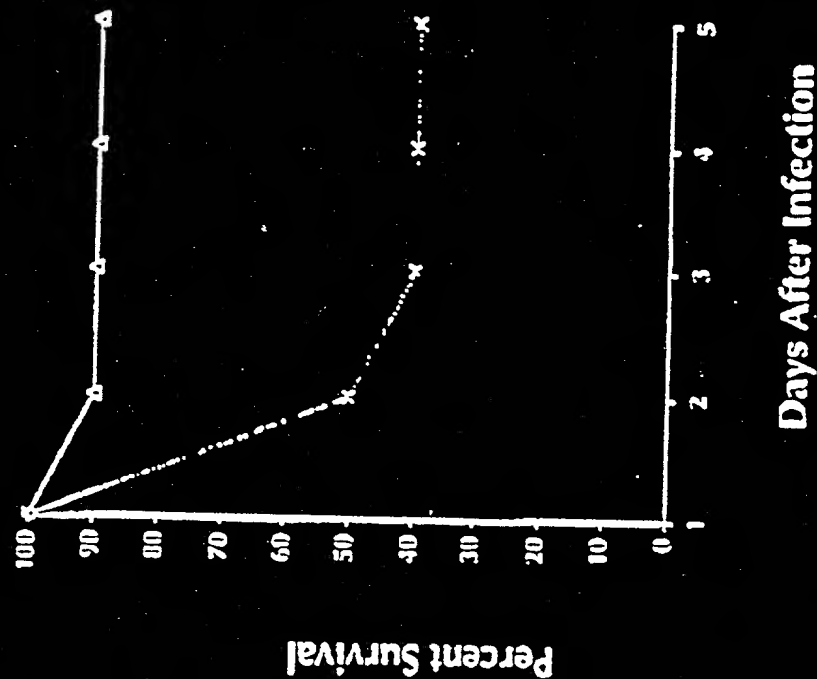
# Bacteremia levels 4 hrs after infection with $3 \times 10^9$ *S.epidermidis*\*

Bactermia expressed as number of bacteria  
isolated on blood agar after 1:1000 dilution  
(Avg  $\pm$  SD)



\* CF-1 mice infected IP with strain Hay-HuMAB given IP x 2

# The Effect of Hu 96-110 on Survival in a Lethal Neonatal *S.epidermidis*\* Sepsis Model: Study II



Survival:  
Hu 96-110 27/30 (90%)  
Saline 12/30 (40%)

—○— Hu 96-110  
...x... Saline Control  
\* ↓ Different SE Strains

Study II:  
Infection - ~5x10<sup>7</sup> SE, SQ (with plastic catheter SQ)  
Lipid Emulsion - 0.2 ml, 20% IP day -1 and + 1, 2  
doses day 0  
HuMAB or Saline- 0.2 ml, IP 30 min before and 24 hrs  
after infection  
Dose: 50-60 mg/kg per dose